Paper No. 33

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte SAMUEL BOGOCH

Appeal No. 1997-2363
Application No.08/031,562

ON BRIEF

Before WILLIAM F. SMITH, SPIEGEL, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 and 2, the only claims under consideration in the application.[1] The claims read as follows:

> 1. A process to inhibit or to destroy cancer cells, to prevent the development of clinical cancer, or if it has already developed, to inhibit or destroy clinical cancer, regardless of cell type, comprising producing and administering a vaccine composed of malignin, Recognin L, Recognin M

[1] Claims 3-8 are also pending but were withdrawn from consideration following a restriction requirement. See Paper No. 6, mailed Dec. 22, 1993.

or other Recognins, or derivatives of these Recognins which contain their immunologic specificity as evidenced by the production of anti-Recognin antibody.

2. A vaccine product, which contains the immunological specificity of malignin, Recognin L or Recognin M, which upon administration to humans or animals, will cause cancer cells, regardless of cell type, to be inhibited or destroyed and will prevent the development of clinical cancer, or if it has already developed, will destroy the cancer cells or inhibit their growth.

Claim 2 stands rejected under 35 U.S.C. § 112, second paragraph, as indefinite.

Claims 1 and 2 stand rejected under 35 U.S.C. § 112, first paragraph, as not enabled by the specification.

We reverse the rejection for indefiniteness but affirm the rejection for non-enablement.

Background

As discussed in Appellant's specification, researchers have theorized that the immune system plays a role in preventing the development of cancer. Page 2. The specification states that this theory has been largely abandoned due to lack of supporting evidence. Pages 2-3.

The specification discloses a group of apparently related tumor antigens, referred to as Recognins and malignin, which are characterized as "general tumor antigens." Page 6. These antigens are reportedly found on tumors derived from a variety of cell types and have identical immunoreactivity. Pages 5-6.

The specification also reports that a Recognin-binding antibody (referred to as "anti-Recognin") is found in healthy individuals and that the level of anti-Recognin increases with age in such individuals, as does the degree of cancer risk. Page 3. The level of anti-Recognin is reported to be highest in individuals who are diagnosed with cancer, and decreases in such individuals when the cancer is successfully treated. Id. The specification also reports experimental results showing that anti-Recognin is cytotoxic and growth-inhibitory to cancer cells in vitro. Id.; see also Figures 1j-1l and Figure 2.

The specification acknowledges that "[t]he notion of a general cancer antigen and antibody was difficult to accept." Page 6. Nevertheless, the specification concludes that the "properties [of anti-Recognin] suggest that anti-Recognin is a general inhibitory transformation antibody whose augmentation may be useful in efforts at the immune prevention and treatment of cancer." Page 5.

Discussion

Claim 1 is directed to a method of preventing the development of clinical cancer, derived from any cell type, or of treating cancer that has already developed, regardless of cell type, by administering a vaccine comprising malignin or a Recognin. Claim 2 is directed to the vaccine product that is administered in the method of claim 1. The examiner rejected claim 2 as indefinite, and rejected both claims as non-enabled.

1. The rejection under 35 U.S.C. § 112, second paragraph.

We begin by considering whether claim 2 complies with the second paragraph of 35 U.S.C. § 112. See In re Moore, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971) (Analysis of a claim under § 112 "should begin with the determination of whether the claims satisfy the requirements of the second paragraph. . . . [T]he claims must be analyzed first in order to determine exactly what subject matter they encompass.").

The examiner rejected claim 2 under 35 U.S.C. § 112, second paragraph, on the basis that "[t]he meaning of the phrase 'immunological specificity' in claim 2 is vague. It is not clear what properties characterize 'immunological specificity.'" Examiner's Answer, page 5. The examiner acknowledged, however, that the same phrase is not indefinite as used in claim 1. Id.

Appellant argues that the phrase "immunological specificity" would be understood by a skilled artisan in the field of immunology to mean that the claimed vaccine product is cross-reactive with antibodies which recognize and interact with Recognin. Reply Brief, page 3.

"The definiteness of the language employed must be analyzed—not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." In re Moore, 439 F.2d at 1235, 169 USPQ at 238. "The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification." Miles

Laboratories Inc. v. Shandon Inc., 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993).

We agree with Appellant that, when read in light of the specification, the claim language is not indefinite. The focus of the entire specification is on antibodies that recognize and bind to Recognins and malignin. These antigens are disclosed to share identical immunoreactivity. In addition, claim 1 specifies that immunological specificity is "evidenced by the production of anti-Recognin antibody."

In view of these disclosures, we are confident that those of ordinary skill in the art, reading claim 2 in light of claim 1 and the specification, would understand the claim language to mean that the vaccine contains a product that is recognized and bound by the same antibodies that recognize and bind to malignin and Recognins. We therefore reverse the rejection under 35 U.S.C. § 112, second paragraph.

2. The rejection under 35 U.S.C. § 112, first paragraph.

Having concluded that both claims are sufficiently definite to pass muster under the second paragraph of 35 U.S.C. § 112, we turn to the issue of enablement. The examiner rejected the claims as not enabled by the specification and provided two separate bases for the rejection. The examiner's first basis of non-enablement was that the specification did not teach how to use the claimed invention because the evidence of record did not show that anti-Recognin actually prevented or treated cancer; i.e., the claimed invention was

inoperative. The examiner's second basis of non-enablement was that the claims were not enabled throughout their full scope.

In our view, these issues cannot properly be separated. A claim does not comply with 35 U.S.C. § 112, first paragraph, unless it is enabled throughout its full scope. A claim that is completely non-enabled and a claim that is enabled throughout only part of its scope are equally unpatentable. In addition, the "scope of enablement" basis in this case is subsumed by the question of whether the claimed invention is operative: if the claimed invention is non-operative, then nothing within its scope is enabled and it necessarily is not enabled throughout its full scope. Therefore, we will consider the examiner's two bases of non-enablement together.

"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement. If the PTO meets this burden, the burden then shifts to the applicant to provide suitable proofs indicating that the specification is indeed enabling." In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

The examiner reasoned that the specification would not have enabled a person of skill in the art to make and use the claimed invention without undue

experimentation "[b]ecause it is unpredictable whether the administration of Recognin would result in the production of antibodies capable of preventing or treating clinical cancer." Examiner's Answer, page 4. That is, the examiner concluded that the evidence of record does not show that administration of the claimed product, or practice of the claimed method, would be likely to successfully prevent or treat cancer.

Appellant points to several lines of evidence as supporting enablement. First, the specification discloses that levels of anti-Recognin antibody are highest in patients diagnosed with cancer, and that anti-Recognin levels decrease on successful treatment of the cancer. Appeal Brief, page 7. Second, Appellant cites actuarial data which show a correlation between the level of patients' anti-Recognin antibody and the length of their survival after cancer diagnosis. Id. Third, Appellant points to published research showing that anti-Recognin binds preferentially to brain glioma cells in vivo in rats. Appeal Brief, page 8. Finally, Appellant points to Figures 1 and 2 as showing that anti-Recognin has cytotoxic and growth inhibitory effects on tumor cells in vitro. Id.[2]

After considering the evidence of record, we agree with the examiner that the specification does not teach those of ordinary skill in the art how to use the claimed invention without undue experimentation. We begin, as always, with the

[2] Appellant also submitted several abstracts, published after the filing date of the instant application, which he characterizes as showing that other peptide tumor antigens have shown positive results in vivo. See the Appeal Brief, page 3. However, enablement is determined as of the filing date of the application. See In re Glass, 492 F.2d 1228, 1232, 181 USPQ 31, 34 (CCPA 1974). Appellant has not explained how the submitted abstracts, which were published in 1994,

language of the claims. Claim 1 is drawn to a method comprising "administering a vaccine," while claim 2 is drawn to a "vaccine product." According to the art-accepted definition, a "vaccine" must protect the vaccinated patient from a specific disease. "[V]accines . . . must by definition trigger an immunoprotective response in the host vaccinated; mere antigenic response is not enough." In re Wright, 999 F.2d at 1562, 27 USPQ2d at 1513. The specification does not define "vaccine" to have a meaning different from the art-accepted meaning. The claims thus are directed to a product and method that protects the vaccinated patient from developing clinical cancer, derived from any cell type, and that is effective in treating developed clinical cancer, derived from any cell type.

To enable the full scope of the instant claims, therefore, the specification must teach those of skill in the art how to prevent or treat clinical cancer, derived from any cell type, by administering anti-Recognin. The guidance provided must be such that a skilled artisan would reasonably conclude that the claimed agent would have the disclosed effect when administered to patients. See Fujikawa v. Wattanasin, 93 F.3d 1559, 1564, 39 USPQ2d 1895, 1899 (Fed. Cir. 1996) ("[T]est results need not absolutely prove that the compound is pharmacologically active. . . . [However], there must be a sufficient correlation between the tests and an asserted pharmacological activity so as to convince those skilled in the art, to a reasonable probability, that the novel compound will exhibit the asserted pharmacological behavior.").

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show enablement of the claimed invention as of March 16, 1993, the filing date of the instant

"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification." In re Wright, 999 F.2d at 1562, 27 USPQ2d at 1513. Exemplary factors to be considered include "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In this case, nearly all of the Wands factors weigh against enablement:

(1) The claims are extremely broad in scope, and read on the prevention or treatment of any type of cancer by administration of malignin, Recognin, or any other molecule that generates cross-reacting antibodies.

(2) No working examples or other detailed guidance are provided. The specification provides only a few prophetic examples with little or no experimental detail. See pages 17-19 of the specification.

(3) The prior art of record discloses no other antibodies to tumor antigens that successfully prevent or treat cancer.

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application. We therefore decline to consider the abstracts.

(4) The basis of the invention's asserted activity is unsupported by scientific evidence. Even Appellant has conceded that "[i]f inhibition of [cancer cell] proliferation is an immune process, as has been theorized, there is no direct evidence in human cancer for such an immune process, and the responsible mechanisms are unknown."[3] Specification, pages 4-5. Thus, the nature of the invention is tentative and scientifically unsupported.

(5) Inventions involving physiological activity are highly unpredictable. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) ("In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.").

On the other hand, the level of skill in the art of cancer treatment is very high. However, on balance, the Wands factors compel a conclusion that the guidance provided by the specification would not have enabled a person of skill in the art to practice the full scope of the claimed invention—i.e., to use anti-Recognin antibodies to prevent or treat any type of cancer—without undue experimentation. The burden is therefore shifted to Appellant "to provide suitable proofs indicating that the specification is indeed enabling." In re Wright, 999 F.2d at 1562, 27 USPQ2d at 1513.

[3] "While it is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works, . . . neither is the patent applicant relieved of the requirement of teaching how to achieve the claimed result, even if the theory of operation is not correctly explained or even understood." Newman v. Quigg, 877 F.2d 1575, 1581-82, 11 USPQ2d 1340, 1345 (Fed. Cir. 1989).

As evidence that the claimed product and method would have been considered likely to be effective in preventing and treating cancer, Appellant cites the cytotoxic and growth inhibiting effects of anti-Recognin seen in vitro. See the Appeal Brief, page 8. However, where in vitro testing is relied upon to establish a pharmacological effect, there must be a known correlation between in vitro test results and in vivo activity. See Fujikawa, 93 F.3d at 1565, 39 USPQ2d at 1900 ("[I]n vitro results, in combination with a known correlation between such in vitro results and in vivo activity, may be sufficient to establish practical utility."). See also Cross v. Iizuka, 753 F.2d 1040, 1061, 224 USPQ 739, 748 (Fed. Cir. 1985) (practical utility shown where application disclosed in vitro activity and prior art disclosed similar in vitro and in vivo pharmacological activity of structurally similar compounds). Appellant has provided no evidence to show that there is a known correlation between the reported in vitro results and in vivo activity, nor are we aware of such a correlation for tumor antigen antibodies. Therefore, the disclosed in vitro results do not establish the utility of the claimed invention.

The other evidence relied on by Appellant also fails to persuade us that the claimed vaccine and method would have been considered likely to be effective in preventing or treating all types of cancer. Appellant points to data showing that levels of anti-Recognin antibody are highest in patients who are diagnosed with cancer, and that the anti-Recognin level decreases on successful treatment of the cancer. Appeal Brief, page 7. Appellant also points to actuarial

data which show a correlation between the level of patients' anti-Recognin antibody and the length of their survival after cancer diagnosis. Id.

Although we note that the second correlation (higher anti-Recognin, longer survival) seems contrary to the first correlation (lower anti-Recognin, successful cancer treatment), we accept them as accurate. Nevertheless, it is a basic scientific principle that correlation does not mean causation. That is, the fact that a higher level of anti-Recognin is associated with longer survival of cancer patients would not lead a skilled artisan to conclude that anti-Recognin causes longer survival. Therefore, a person of ordinary skill in the art would not expect that artificially increasing the level of anti-Recognin would have the effect of increasing a patient's survival time.

Appellant also points to published data showing that anti-Recognin binds preferentially in vivo to brain glioma cells in rats. Appeal Brief, page 8. These data, however, show only that anti-Recognin binds to glioma cells; they do not show that the binding of anti-Recognin had any effect on the cells whatsoever. The claimed invention is directed to prevention and treatment of cancer in patients. To have these activities, anti-Recognin must do more than bind to cancer cells in vivo; it must kill them, or at a minimum stop them from growing further. The cited evidence does not show that anti-Recognin has any such effect.

Finally, we note that the facts of this case distinguish it from In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995). In Brana, the claims were

directed to chemical compounds that were asserted to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437. The applicants reported in vitro tests showing that the claimed compounds were effective antitumor agents, see id. at 1563, 34 USPQ2d at 1438, and the prior art disclosed structurally similar compounds which had been "proven in vivo to be effective as chemotherapeutic agents against various tumor models." Id. at 1566, 34 USPQ2d at 1441.

Thus, Brana presented a situation in which the disclosed in vitro results were accompanied by a known correlation between in vitro and in vivo pharmacological activity. The in vitro results therefore were sufficient to establish the utility of the claimed compounds. Here, by contrast, the prior art discloses no tumor antigen antibodies that are effective in vivo as vaccines for treating or preventing cancer. Thus, the facts of this case do not provide the required correlation between in vitro and in vivo results that was present in Brana.

Thus, upon consideration of the record as a whole, we conclude that a preponderance of the evidence supports the examiner's conclusion that undue experimentation would have been required to practice the full scope of the claimed invention. We therefore affirm the rejection for non-enablement.

Summary

We reverse the rejection of claim 2 under 35 U.S.C. § 112, second paragraph, but we affirm the rejection of claims 1 and 2 under 35 U.S.C. § 112, first paragraph, because the specification does not adequately teach those of skill in the art how to make and use the full scope of the claimed invention.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

WILLIAM F. SMITH
Administrative Patent Judge

CAROL A. SPIEGEL
Administrative Patent Judge

ERIC GRIMES
Administrative Patent Judge

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